

EPITHELIOMATOSIS OF THE BREAST.

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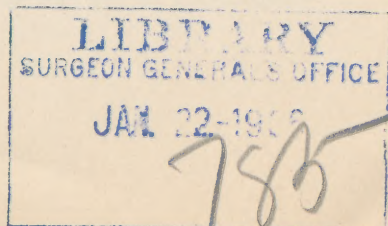
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UNDER the title of Paget's disease is described a chronic pathologic process, involving the skin of the nipple and the areola, accompanied by a carcinoma in the mammary gland. This affection is, consequently, made up of a pathologic change in the skin and a lesion of the mammary gland. Besnier has given this pathologic complexus the name of epitheliomatosis of the breast, which term we have here adopted as defining the nature of the malady more lucidly.

In 1874, Sir James Paget first gave to the medical world a description of this rather peculiar disease, and again, in 1890, Wickham, of Paris, published his important "Mémoire," giving a detailed clinical description of the affection. Wickham emitted the opinion that the dermatitis could go through its entire evolution without any carcinomatous changes taking place in the gland, and, following out Darier's experiments and histologic studies, he concluded in favor of the theory of the presence of psorospermic bodies in the diseased cutaneous structures.

The psorospermic nature of the bodies described by Darier is at the present time denied, and the opinion emitted by Karg is probably correct,—namely, that this dermatitis is epitheliomatous in nature, or at least is susceptible to become so. Schulten believes that epitheliomatosis is a disease similar to carcinoma, but not identical. Jamieson, Russell, and many others have pretty positively proven the non-psorospermic nature of this affection.



The following brief account of a case of epitheliomatosis, which was recently under our care, may, we trust, help to increase our knowledge of this rather rare disease, and afterwards a few general remarks will, perhaps, not be out of place.

The patient, a woman of sixty-two years, and mother of several children, applied at the writer's clinic, at the Tremont Dispensary, in the latter part of November, 1897. She was a stout subject, with an excellent personal history. For the past eight months the patient stated that the nipple of her left breast had been, as she expressed it, inflamed, and had caused great inconvenience from the pruritus to which it gave rise.

Examination of the right breast was negative. The entire areola of the left breast presented a bright-red, moist surface, the process being distinctly limited to the areola. The nipple was not retracted nor deformed. No distinct ulceration could be detected, but in some spots the epidermis appeared eroded. The skin of the breast was normal and no enlarged subcutaneous veins were visible. The surface of the dermatitis gave rise to a rather sticky, slightly yellow secretion.

Directly in the midst of the glandular tissue, and *situated exactly under the region of the areola*, an indolent mass, which appeared by palpation to be distinctly limited to the gland, could be felt, and seemed about the size of a large walnut. Two very hard, small lymphatic glands were detected in the left axilla. The supraclavicular glands were not enlarged. A diagnosis of Paget's disease was made and removal of the breast advised.

On December 12, 1897, we removed the breast and cleaned out the axilla. The patient made an excellent and uninterrupted recovery, and was discharged in three weeks.

We carefully examined the specimen with the following results: Microscopic examination of the neoplasm of the gland showed that in structure it was an ordinary carcinoma.

The epidermis of the areola presented different aspects. In the less diseased parts there was a considerable elongation of the papillæ. The cells of the surface were replaced by polygonal elements, their nuclei being very small. At other points the epidermis was rather thin and the papillæ were absent. Gradually the so-called bodies of Darier were seen in the middle and deep layers of the rete mucosum of Malpighi, and in the spots

where their development was the most marked they penetrated the interpapillary columns.

The cavities present in the epidermis contained *débris* of all kinds, as well as cocci and a few bacilli. In some places the epidermis was quite changed, and small cells of varied shape, with a distinct outline and an opaque nucleus, were seen between the epithelial cells. We consider these elements as in all probability lymphatic in nature.

In the dermis an extremely deep and abundant proliferation of embryonal cells was found in certain parts; their nuclei were granular, and the elements took the stain well. In all the sections examined, the tissue of the neoplasm of the gland was separated from the cutaneous structure by a rather thin layer of connective tissue.

For a moment let us consider the pathology of the disease under consideration. Macroscopically, the epidermis is only slightly increased in thickness, and, generally speaking, the lesion is very superficial. There is no underlying infiltration nor induration. As to the nipple, in those cases in which it has disappeared, either by destruction or retraction, it is replaced by a mass of hard tissue, having the usual appearance of carcinoma.

Microscopically, Darier and Wickham described the bodies that they considered were psorospermic in nature, but which are in reality only a change in the cells. Butlin pointed out that there was a thickening of the layer of crenated cells, as well as an increase in the papillæ and subepidermic infiltration. Duhring and Weld found the same general changes, and also the presence of cell agglomerations, analogous to the horny globes met with in epithelioma. They found that the dermatitis begins abruptly on the borders, and as the lesion extends from the periphery towards the centre, the areola is deprived of its epithelial covering. They also insist on the vacuolar changes. Unna is also of the opinion that the pathologic changes, making up the so-called psorospermic bodies, are due to a particular kind of degeneration of the prickle-cells, and is a sort of œdema of the epithelium.

The papillæ are infiltrated and round, while on the borders of the interpapillary columns, disseminated, round, or oval, clear spaces are to be seen, and which appear to be of an epitheliomatous nature under a high power. They contain very large nuclei, and are quite rich in chromatin. Many are to be found undergoing mitosis, while in each interpapillary column about one-fourth of the cells present a karyokinesis.

The œdematous cells are distinguished from the others by their nuclei, which are very deeply stained, and are surrounded by a poorly stained, protoplasmic areola. Sometimes the œdematous cells are disseminated uniformly throughout, and the rete mucosum of Malpighi is tumefied. The lacunæ are differentiated from the intercellular vesicles by the fact that there are no dilated plasmatic spaces, but a real loss of substance is present, resulting from an intense liquefaction of the cell protoplasm.

Unna differentiates the lesion in question from a reticulated degeneration of the epidermis by the fact that the uniting filaments have entirely disappeared, while their traces are present in the latter lesion.

Karg states that he has distinctly seen the diseased epithelium pass through the basement layer and extend throughout the dermis in a most atypical manner, so that the epidermic degeneration always ended in a carcinomatous formation.

Banti has described Darier's bodies carefully, as well as the capsules, intracapsular bodies, and the endogenic formation of the latter. He believes in the psorospermic nature of the bodies, but does not consider them as parasitic. Neisser and Barduzzi accept the psorospermic theory, while Ravolgi states that the dermatitis is not, in the beginning, a true epithelioma, but that later on it may become carcinomatous.

Briefly, then, the lesions met with are as follows: On the very thickened borders of the epidermis, Darier's bodies are present. When they are typical, these figures are apparently a sort of rounded cyst, clear at their periphery, with

their limiting membrane, occasionally presenting flattened nuclei, and containing or rather including another cell with its protoplasm and nucleus. The protoplasm is only slightly stained, while the nucleus, which is always large and well stained, shows signs of karyokinesis.

Towards the centre of the lesion these bodies are more numerous, and at last completely obstruct the interpapillary spaces. The entire epithelium is then composed of pseudocystic cells, which are completely wanting in uniting filaments. These changes are quite as marked at the basal membrane, near the generative layer, as in the midst of the interpapillary columns.

During all this process, all keratogenic evolution has entirely disappeared. A kind of fibrinous exudate is immediately superposed on the rete mucosum of Malpighi, and at last the exudate disappears, the epidermis undergoes a complete abrasion, and is only represented by the decapitated trunks of the interpapillary columns. Below, the reactional infiltration is both limited and intense, and is seen as a closely packed accumulation of plasmatic cells.

At certain points the diseased epithelium undergoes most important changes. The papillæ become elongated, deformed, and present a bifurcation; the basement membrane, being broken through by the vacuolated epithelium, sets up a perfectly distinct carcinomatous infiltration. The stroma is fibrous, while the alveolæ are filled with polygonal epithelial cells, with an oval nucleus and rather poorly off in chromatin. Many of them are undergoing karyokinesis. The cells are uniformly filled with a granular protoplasm.

In the deep structures most observers have found an obstruction of the excretory glands, but this is not invariably the case. Although the carcinoma of the gland may resemble a glandular epithelioma, many specimens only show inflammatory changes in the canals of the gland, while among them may be seen disseminated neoplastic alveolæ.

As Fisse has pointed out, epitheliomatosis of the breast is an acantholytic process from the onset, and commences in

both the deep and middle layers of the epidermis, firstly by the disappearance of the uniting filaments and a pronounced tumefaction of one or several cells. Their protoplasma becomes contracted and disappears, while in their interior other cells are seen, probably born by an endogenic process of division.

The acantholysis and cell tumefaction finally invade the entire epidermis, and under the influence of this lesion the epidermis loses all power of accomplishing a keratogenic evolution; it is thus without protection, and consequently undergoes a partial destruction.

In some cases the altered epithelium takes on the properties of a malignant tissue, breaking into the dermis and invading the latter in the form of a carcinomatous infiltration, the alveolæ of which are filled with cells having a cutaneous origin.

As to the manner in which the pseudocystic formations take place, Fisse says that an initial change of a ferment type may occur in the exoplasma of Malpighi's cells. The exoplasma loses its uniting filaments and becomes of such consistency that it forms a true enveloping membrane. Then the protoplasm condenses around the nucleus, and as the latter has not lost its power of multiplication, when the mass of protoplasm is ready to divide it cannot break the exoplastic membrane of the mother cell any more than can the daughter plaque. In other words, a process of granulation takes place within, because the elements of the granulation tissue are incarcerated, on account of the change in the maternal exoplasma.

Epitheliomatosis of the breast is not an infrequent affection, and, according to the cases recorded thus far, may occur between the ages of twenty-two and seventy-two years. The disease has been met with in the male breast, and in a case reported by Crocker the scrotum and penis were also the seat of the malady. Other parts of the body have been attacked by it.

The affection rarely attacks both breasts, but Besnier has

pointed out that when only one breast was diseased the other nipple (the healthy one) often presents keratogenic productions. The latter may be due to want of cleanliness, in which case these productions would appear to be an etiological factor and not an early symptom of the affection.

So long as the epidermis of the areola has its keratinized covering, the disease may be considered as at its *début*, and it is not at all certain that every female who presents adherent and persistent scabs covering the areola will, of necessity, develop an epitheliomatosis. It is well known that the period of latency may last for many years, but there are instances in which it extended over only a few months.

The affection manifests itself by an excoriation of the integument, be it traumatic or otherwise. There is not a tendency for the nipple to retract at an early date, and in the case here reported, and in another recorded by Fisse, the nipple was not retracted, even although the gland was well invaded by the carcinoma.

When the initial point becomes definitely excoriated, and the parts covered by scabs become red and present a moist surface, completely deprived of all keratinization, it may be said that the affection has developed, but, generally speaking, there is no true ulceration present.

The disease once under way, occupies the entire areola and nipple, the parts being limited by normal skin. The lesion only infrequently extends beyond the areola, but some instances are on record in which it extended eccentrically over the greater part of the breast or even the thorax and arm. There is only a very slight induration of the patch, probably because the integument only is affected, there being only a slight involvement of the subepithelial connective tissue.

The most frequent subjective symptoms are pruritus, pain, more especially during lactation, dragging or burning sensation, etc.

As is well known, when epitheliomatosis occurs in the breast, the presence of a carcinoma in the latter is most sure

to appear sooner or later. The neoplasm develops in various forms, sometimes as scirrhus, with several foci scattered through the tissues of the gland; at others, it takes the form of an ordinary carcinoma. In most instances the carcinoma is quite independent from the dermatitis, but the neoplasm may extend towards the surface and invade the diseased epidermis from below. When this occurs we have a true carcinomatous ulceration, which interrupts the continuity of the diseased integument. The ulcerations usually start at the orifices of the galactophores and infrequently an ulcerating epitheliomatosis may arise on the surface.

The carcinoma is not typical in each and every case, and Fisse reports one example in which there was undoubted adenomatous formation, the adenoma being reproduced in an accessory breast in the axilla. The symptoms are those of ordinary carcinoma of the breast with infection of the lymphatic glands of the axilla and pectoralis major, when the case has advanced.

Epitheliomatosis would in all probability continue indefinitely if the carcinoma did not appear. Pregnancy and lactation, as might be expected, appear to increase the rapidity of its progress, and when the carcinomatous formation arises in a young subject, it takes on its usual excessive malignant characters. In elderly people the neoplasm is usually of the atrophic scirrhus type.

In considering the prognosis, we should make two distinct types of the affection. Among the first are those instances in which the malignant transformation has not as yet appeared, and it is evident that the prognosis, although reserved, is favorable, if by proper treatment the lesion of the areola can be perhaps cured.

When the patient presents a malignant transformation in the gland, the prognosis is that of carcinoma in general, and is naturally graver in direct relation to the length of time the neoplasm has been present and in indirect relation to the age of the subject.

A differential diagnosis of epitheliomatosis of the breast

is not difficult to make, but when it is localized to the nipple, it may be mistaken for an eczema, especially the seborrhœic form. In the latter type the scabs are yellower, more greasy, and less adherent, while the prognosis is perfectly benign.

A syphilitic initial sclerosis of the superficial type might be mistaken for an epitheliomatosis of the breast, especially when the latter is in its early stage, and consequently limited in extent, but the initial sore will rarely involve the entire nipple; it is always accompanied by an induration, and its surface is less papillomatous than in Paget's disease. The appearance of secondary lesions will soon disperse all doubt as to the nature of the local lesion.

As to treatment, we believe, contrary to the opinion of Mr. Roger Williams and some other authorities, that every time the diagnosis of epitheliomatosis of the breast is made with certainty, removal of the breast should be done without delay, and we agree with Mr. Sheild when he says that it is probable that excision of the nipple and areola or nipple alone, without removal of the breast, is not sufficient to insure the patient against the later appearance of mammary carcinoma. We can, it is true, cure the lesions of the areola and nipple by medical treatment in many cases, but the danger of malignant transformation in the gland would lead the writer to amputate the breast in every case, and we strongly protest against the treatment of this affection by the dermatologist.

LITERATURE CONSULTED.

- Thin: Transactions of the Pathological Society of London, 1881.
 Russell: British Medical Journal, January 7, 1888.
 Wickham: *Maladie de la Peau, dite Maladie de Paget*, Thèse, Paris, 1890.
 Annales de Dermatologie, 1890, 1891, and 1896.
 Jamieson: Diseases of the Skin, 3d edition, 1891.
 Karg: Deutsche Zeitschrift für Chirurgie, 1892.
 Jackson: Journal of Cutaneous and Venereal Disease, 1896.
 Fisse: Thèse de Toulouse, 1897.
 S. W. Gross: Tumors of the Mammary Gland, 1880, pp. 28-31.
 W. Roger Williams: Diseases of the Breast, 1894, pp. 393-402.
 Bowlby: Surgical Pathology, 1895, pp. 487-489.
 A. Marmaduke Sheild: Diseases of the Breast, 1898, pp. 153-166.

